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 NEWS  2  AUG 10  Time limit for inactive STN sessions doubles to 40
                  minutes
 NEWS  3  AUG 18  COMPENDEX indexing changed for the Corporate Source
                  (CS) field
 NEWS  4  AUG 24  ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
 NEWS  5  AUG 24  CA/CAplus enhanced with legal status information for
                  U.S. patents
 NEWS  6  SEP 09  50 Millionth Unique Chemical Substance Recorded in
                  CAS REGISTRY
 NEWS  7  SEP 11  WPIDS, WPINDEX, and WPIX now include Japanese FTERM
                  thesaurus

 NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
              AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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FILE 'HOME' ENTERED AT 23:09:45 ON 11 OCT 2009

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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STRUCTURE FILE UPDATES: 9 OCT 2009 HIGHEST RN 1187817-34-0
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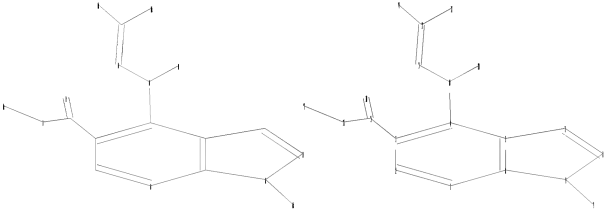

chain nodes :
10 11 12 13 14 15 16 17 18 19 20
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
3-15 4-10 9-19 10-11 10-20 11-12 12-13 12-14 15-16 15-18 16-17
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
4-10 5-7 6-9 7-8 8-9 9-19 10-11 11-12 12-13 12-14 15-16 15-18 16-17
exact bonds :
3-15 10-20
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS

L1 STRUCTURE UPLOADED

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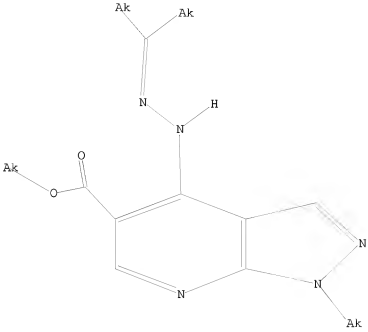

Structure attributes must be viewed using STN Express query preparation.

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FULL SEARCH INITIATED 23:11:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 119 TO ITERATE

100.0% PROCESSED 119 ITERATIONS 28 ANSWERS
SEARCH TIME: 00.00.01

L2 28 SEA SSS FUL L1

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FULL ESTIMATED COST 185.88 186.32

FILE 'CAPLUS' ENTERED AT 23:11:38 ON 11 OCT 2009
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FILE COVERS 1907 - 11 Oct 2009 VOL 151 ISS 16
FILE LAST UPDATED: 9 Oct 2009 (20091009/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2009.

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substance identification.

=> s l2
L3 167 L2

=> s l3 and cognition
19561 COGNITION
L4 6 L3 AND COGNITION

=> d l4 1-6 ibib abs hitstr

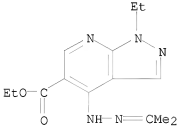
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:827349 CAPLUS
DOCUMENT NUMBER: 149:167804
TITLE: Etazolate, a neuroprotective drug linking GABAA receptor pharmacology to amyloid precursor protein processing
AUTHOR(S): Marcade, Maryline; Bourdin, Jerome; Loiseau, Nadia; Peillon, Helene; Rayer, Aurelie; Drouin, Dominique; Schweighoffer, Fabien; Desire, Laurent
CORPORATE SOURCE: Department of Neurology, ExonHit Therapeutics, Paris, Fr.
SOURCE: Journal of Neurochemistry (2008), 106(1), 392-404
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pharmacol. modulation of the GABAA receptor has gained increasing attention as a potential treatment for central processes affected in Alzheimer disease (AD), including neuronal survival and cognition . The proteolytic cleavage of the amyloid precursor protein (APP) through the α-secretase pathway decreases in AD, concurrent with cognitive impairment. This APP cleavage occurs within the β-amyloid peptide (Aβ) sequence, precluding formation of amyloidogenic peptides and leading to the release of the soluble N-terminal APP fragment (sAPPα) which is neurotrophic and procognitive. In this study, we show that at nanomolar-low micromolar concns., etazolate, a selective GABAA receptor modulator, stimulates sAPPα production in rat cortical neurons and in guinea pig brains. Etazolate (20 nM-2 μM) dose-dependently protected rat cortical neurons against Aβ-induced toxicity. The neuroprotective effects of etazolate were fully blocked by GABAA receptor antagonists indicating that this neuroprotection was due to GABAA receptor signaling. Baclofen, a GABAB receptor agonist failed to inhibit the Aβ-induced neuronal death. Furthermore, both pharmacol. α-secretase pathway inhibition and sAPPα immunoneutralization

approaches prevented etazolate neuroprotection against Aβ, indicating that etazolate exerts its neuroprotective effect via sAPPα induction. Our findings therefore indicate a relation between GABAA receptor signaling, the α-secretase pathway and neuroprotection, documenting a new therapeutic approach for AD treatment.

IT 51022-77-6, Etazolate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(etazolate, neuroprotective drug linking GABAA receptor pharmacol. to amyloid precursor protein processing)

RN 51022-77-6 CAPLUS

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:493012 CAPLUS

DOCUMENT NUMBER: 148:509885

TITLE: Compositions and methods for treating neurological disorders or damage

INVENTOR(S): Diamandis, Phedias; Tyers, Mike; Dirks, Peter B.

PATENT ASSIGNEE(S): Can.

SOURCE: Can. Pat. Appl., 3pp.
CODEN: CPXXEB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2606658	A1	20080413	CA 2007-2606658	20071012
US 20090076019	A1	20090319	US 2007-871562	20071012

PRIORITY APPLN. INFO.: US 2006-851615P P 20061013

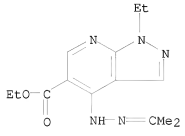
AB The invention relates to a clonogenic neurosphere assay to carry out high throughput screens (HTS) to identify potent and/or selective modulators of proliferation, differentiation and/or renewal of neural precursor cells, neural progenitor cells and/or self-renewing and multipotent neural stem cells (NSCs). The invention also relates to compns. comprising the identified modulators and methods of using the modulators and compns., in particular to treat neurol. disorders (e.g. brain or CNS cancer) or damage.

IT 35838-58-5, Etazolate hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(screening for compns. and methods for treating neurol. disorders or damage with modulators of neural stem cells)

RN 35838-58-5 CAPLUS

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester, hydrochloride (1:1) (CA INDEX NAME)



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OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:874191 CAPLUS

DOCUMENT NUMBER: 147:227213

TITLE: Compositions and methods using pyrimidine-4,6-diamine derivative Ih (hyperpolarization-activated cationic current) channel blockers for treating cognitive disorders

INVENTOR(S): Arnsten, Amy F. T.; Wang, Min; McCormick, David A.; Ramos, Brian P.

PATENT ASSIGNEE(S): Yale University, USA

SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007089774	A2	20070809	WO 2007-US2527	20070131
WO 2007089774	A3	20071115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

EP 1993612	A2	20081126	EP 2007-762676	20070131

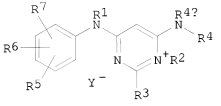
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,

BA, HR, MK, RS

US 20090221610	A1	20090903	US 2008-86658		20081222
PRIORITY APPLN. INFO.:			US 2006-763802P	P	20060131
			WO 2007-US2527	W	20070131

OTHER SOURCE(S): MARPAT 147:227213

GI



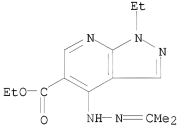
I

AB The invention discloses the use of inhibitors or blockers of Ih (hyperpolarization-activated cationic current) channels in the treatment of cognitive disorders. In preferred aspects of the invention, an effective amount of a compound I [R1 = H, (un)substituted C1-3 alkyl; R2 = (un)substituted C1-3 alkyl; R3 = H, (un)substituted C1-3 alkyl, halo, O(C1-3)alkyl; R4 = (un)substituted C1-6 alkyl, C(O)-(C1-5)alkyl, etc.; R4a = H, (un)substituted C1-6 alkyl; R5-R7 = H, halo, (un)substituted C1-6 alkyl, etc.; Y- = anion of pharmaceutically acceptable salt]; or a solvate or polymorph thereof, is administered to a patient, optionally, in combination with guanfacine and/or chelerythrine, and a pharmaceutically acceptable carrier, additive or excipient.

IT 51022-77-6, Etazolate
RL: PAC (Pharmacological activity); BIOL (Biological study)
(pyrimidinediamine derivative Ih channel blockers for treatment of cognitive disorders)

RN 51022-77-6 CAPLUS

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester (CA INDEX NAME)



L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	2005:216623 CAPLUS
DOCUMENT NUMBER:	142:274015
TITLE:	Treatment or prevention of vascular disorders with cyclooxygenase 2 (COX-2) inhibitors in combination with cyclic AMP-specific phosphodiesterase inhibitors
INVENTOR(S):	Taylor, Duncan P.
PATENT ASSIGNEE(S):	Pharmacia Corporation, USA
SOURCE:	PCT Int. Appl., 90 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020926	A2	20050310	WO 2004-US28118	20040827
WO 2005020926	A3	20050506		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

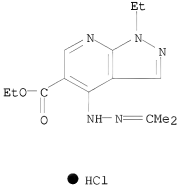
US 20050187278	A1	20050825	US 2004-927198	20040826
PRIORITY APPLN. INFO.:			US 2003-498529P	P 20030828
			US 2003-513099P	P 20031021

AB A method is described for the prevention and/or treatment of vascular disorders and vascular disorder-related complications in a subject, the method comprising administering to the subject a COX-2 inhibitor in combination with a cAMP-specific PDE inhibitor. Also described are therapeutic and pharmaceutical compns. and kits that are useful in the invention. Preparation of celecoxib is also described.

IT 35838-58-5, Etazolate hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor combination with cAMP-specific phosphodiesterase inhibitor for treatment or prevention of vascular disorder)

RN 35838-58-5 CAPLUS

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester, hydrochloride (1:1) (CA INDEX NAME)



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:588 CAPLUS

DOCUMENT NUMBER: 142:86671
TITLE: Methods and compositions for the treatment of cognitive deficiencies with ligands for the benzodiazepine peripheral receptor
INVENTOR(S): Schweighoffer, Fabien; Desire, Laurent; Resink, Annelies
PATENT ASSIGNEE(S): Exonhit Therapeutics S. A., Fr.
SOURCE: Fr. Demande, 34 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2856595	A1	20041231	FR 2003-7824	20030627
FR 2856595	B1	20080530		
AU 2004251466	A1	20050106	AU 2004-251466	20040625
CA 2528284	A1	20050106	CA 2004-2528284	20040625
WO 2005000302	A1	20050106	WO 2004-FR1630	20040625
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EP 1638559	A1	20060329	EP 2004-767477	20040625
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CN 1812786	A	20060802	CN 2004-80018148	20040625
JP 2007520427	T	20070726	JP 2006-516332	20040625
IN 2005DN05464	A	20070817	IN 2005-DN5464	20051128
US 20060142326	A1	20060629	US 2005-560774	20051214

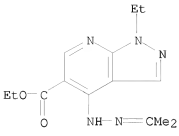
PRIORITY APPLN. INFO.:
FR 2003-7824 A 20030627
WO 2004-FR1630 W 20040625

AB The present invention relates to methods to improve, increase or facilitate the cognitive ability of subjects afflicted with neurodegenerative disorders. The invention more particularly involves ligands for the benzodiazepine peripheral receptor, preferably ligands of the pyrazolopyridine family, for the improvement of cognitive abilities in subjects afflicted with neurodegenerative disorders, particularly those with Alzheimer's disease.

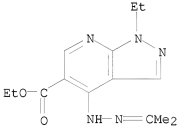
IT 51022-77-6, Etazolate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as a ligand of the peripheral benzodiazepine receptor; methods and compns. for treatment of cognitive deficiencies with ligands for benzodiazepine peripheral receptor)

RN 51022-77-6 CAPLUS

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester (CA INDEX NAME)



IT 35838-58-5, SQ 20009
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for treatment of cognitive deficiencies with ligands for benzodiazepine peripheral receptor)
RN 35838-58-5 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester, hydrochloride (1:1) (CA INDEX NAME)



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OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:453015 CAPLUS
DOCUMENT NUMBER: 141:17632
TITLE: Methods and agents elevating cAMP and calcium ion for increasing neurogenesis
INVENTOR(S): Bertilsson, Goran; Erlandsson, Rikard; Frisen, Jonas; Haegestrand, Anders; Heidrich, Jessica; Hellstrom, Kristina; Haggblad, Johan; Jansson, Katarina; Kortesmaa, Jarkko; Lindquist, Per; Lundh, Hanna; McGuire, Jacqueline; Mercer, Alex; Njberg, Karl; Ossoinak, Amina; Patrone, Cesare; Ronnholm, Harriet; Zachrisson, Olof; Wikstrom, Lilian
PATENT ASSIGNEE(S): Neuronova AB, Swed.
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045592	A2	20040603	WO 2003-IB5311	20031120
WO 2004045592	A3	20041104		
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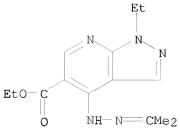
PRIORITY APPLN. INFO.:	US 2002-427912P	P	20021120
	US 2003-718071	A	20031120
	WO 2003-IB5311	W	20031120
	US 2004-850055	A	20040519
	WO 2004-IB4451	W	20041119

AB The invention discloses methods for promoting neurogenesis by contacting neuronal tissue with intracellular cAMP-elevating agents and intracellular calcium ion-elevating agents. Agents for promoting neurogenesis are also disclosed.

IT 35838-58-5, Etazolatehydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cAMP-elevating and calcium ion-elevating compds. for increasing neurogenesis)

RN 35838-58-5 CAPLUS

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester, hydrochloride (1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

=> d his]
'HIS]' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
SCAN must be entered on the same line as the DISPLAY,
e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, CLASS

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IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
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containing hit terms
HITRN ------- HIT RN and its text modification

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HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
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specification.

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to view a specified Accession Number.
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The following are valid formats:

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ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
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OBIB -------- AN, plus Bibliographic Data (original)
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HIT --------- Fields containing hit terms
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OCC --------- Number of occurrence of hit term and field in which it occurs

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information will be displayed in the same order as the format
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DN   149:167804
TI   Etazolate, a neuroprotective drug linking GABAA receptor pharmacology to
     amyloid precursor protein processing
AU   Marcade, Maryline; Bourdin, Jerome; Loiseau, Nadia; Peillon, Helene;
     Rayer, Aurelie; Drouin, Dominique; Schweighoffer, Fabien; Desire, Laurent
CS   Department of Neurology, ExonHit Therapeutics, Paris, Fr.
SO   Journal of Neurochemistry (2008), 106(1), 392-404
     CODEN: JONRA9; ISSN: 0022-3042
PB   Blackwell Publishing Ltd.
DT   Journal
LA   English
OSC.G   2     THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
RE.CNT  59    THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L5   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2009 ACS on STN
AN   2008:827349  CAPLUS
DN   149:167804
TI   Etazolate, a neuroprotective drug linking GABAA receptor pharmacology to
     amyloid precursor protein processing
AU   Marcade, Maryline; Bourdin, Jerome; Loiseau, Nadia; Peillon, Helene;
     Rayer, Aurelie; Drouin, Dominique; Schweighoffer, Fabien; Desire, Laurent
CS   Department of Neurology, ExonHit Therapeutics, Paris, Fr.
SO   Journal of Neurochemistry (2008), 106(1), 392-404
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RE.CNT  59    THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L5   ANSWER 2 OF 7  CAPLUS  COPYRIGHT 2009 ACS on STN
AN   2008:91629  CAPLUS
DN   148:136029
TI   Methods and tools for the therapy of neurodegenerative pathologies
IN   Schweighoffer, Fabien; Desire, Laurent; Bourdin, Jerome
PA   Exonhit Therapeutics SA, Fr.
SO   PCT Int. Appl., 38 pp.
     CODEN: PIXXD2
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LA   French
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     WO 2007-FR51706     W      20070720

L5   ANSWER 3 OF 7  CAPLUS  COPYRIGHT 2009 ACS on STN
AN   2005:588  CAPLUS
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DN 142:86671
TI Methods and compositions for the treatment of cognitive deficiencies with ligands for the benzodiazepine peripheral receptor
IN Schweighoffer, Fabien; Desire, Laurent; Resink, Annelies
PA Exonhit Therapeutics S. A., Fr.
SO Fr. Demande, 34 pp.
CODEN: FRXXBL
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LA French
FAN.CNT 1

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	WO 2004-FR1630	W	20040625		

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RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:934227 CAPLUS
DN 141:388737
TI Phosphodiesterase 4B gene mutations in diagnosis of brain disorders and PDE4B inhibitors for treatment of brain disorders
IN Ait, Ikhlef Ali; Resink, Annelies; Schweighoffer, Fabien
PA Fr.
SO U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 983,754.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

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     US 2004-486639       A2    20040212
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L5   ANSWER 5 OF 7  CAPLUS  COPYRIGHT 2009 ACS on STN
AN   2004:453015  CAPLUS
DN   141:17632
TI   Methods and agents elevating cAMP and calcium ion for increasing
     neurogenesis
IN   Bertilsson, Goran; Erlandsson, Rikard; Frisen, Jonas; Haegestrand, Anders;
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PA   Neuronova AB, Swed.
SO   PCT Int. Appl., 77 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
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PRAI US 2002-427912P      P     20021120
     US 2003-718071       A     20031120
     WO 2003-IB5311       W     20031120
     US 2004-850055       A     20040519
     WO 2004-IB4451       W     20041119
OSC.G   6     THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

L5   ANSWER 6 OF 7  CAPLUS  COPYRIGHT 2009 ACS on STN
AN   2003:154633  CAPLUS
DN   138:203092
TI   A gene for a phosphodiesterase isoenzyme playing a role in excitotoxicity
     in the etiology of neurodegenerative disease
IN   Aiet Ikhlef, Ali; Resink, Annelies; Schweighoffer, Fabien
PA   Exonhit Therapeutics S.A., Fr.
SO   PCT Int. Appl., 64 pp.
     CODEN: PIXXD2
DT   Patent
LA   French
FAN.CNT 3
     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
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PI   WO 2003016563        A2     20030227    WO 2002-FR2861         20020813
     WO 2003016563        A3     20040401
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
              UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
              FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
              CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2828693           A1     20030221    FR 2001-10819          20010814
     FR 2828693           B1     20040618
     CA 2457611           A1     20030227    CA 2002-2457611        20020813
     AU 2002339017        A1     20030303    AU 2002-339017         20020813
     AU 2002339017        B2     20071101
     EP 1417349           A2     20040512    EP 2002-777405         20020813
     EP 1417349           B1     20081119
          R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     CN 1541278           A      20041027    CN 2002-815840         20020813
     JP 2005500066        T      20050106    JP 2003-521870         20020813
     NZ 530939            A      20061130    NZ 2002-530939         20020813
     EP 1982704           A2     20081022    EP 2008-160783         20020813
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     EP 1982704          A3    20081217
        R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT,
            LI, LU, MC, NL, PT, SE, SK, TR
     AT 414790           T     20081215    AT 2002-777405         20020813
     ES 2316625          T3    20090416    ES 2002-777405         20020813
     US 20040219552      A1    20041104    US 2004-486639         20040212
     US 20050043319      A1    20050224    US 2004-857455         20040601
PRAI FR 2001-10819       A     20010814
     US 2001-983754      A2    20011025
     EP 2002-777405      A3    20020813
     WO 2002-FR2861      W     20020813
     US 2004-486639      A2    20040212
OSC.G   5     THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
RE.CNT  5     THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5   ANSWER 7 OF 7  CAPLUS  COPYRIGHT 2009 ACS on STN
AN   2000:62023  CAPLUS
DN   132:216984
TI   Interaction of various intracellular signaling mechanisms involved in
     mononuclear phagocyte toxicity toward neuronal cells
AU   Klegeris, Andis; McGeer, Patrick L.
CS   Kinsmen Laboratory of Neurological Research, University of British
     Columbia, Vancouver, BC, V6T 1Z3, Can.
SO   Journal of Leukocyte Biology (2000), 67(1), 127-133
     CODEN: JLBIE7; ISSN: 0741-5400
PB   Federation of American Societies for Experimental Biology
DT   Journal
LA   English
OSC.G   32    THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)
RE.CNT  41    THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=>
=>  s pde4
L6        1720 PDE4

=> s l6 and alzheimer and cognition
         59100 ALZHEIMER
         19561 COGNITION
L7          51 L6 AND ALZHEIMER AND COGNITION

=> s pde4b
L8         287 PDE4B

=> s l8 and alzheimer and cognition
         59100 ALZHEIMER
         19561 COGNITION
L9           0 L8 AND ALZHEIMER AND COGNITION

=> d l7 30-51 ibib abs

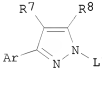
L7   ANSWER 30 OF 51  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2006:380892  CAPLUS
DOCUMENT NUMBER:          144:432795
TITLE:                    Preparation of pyrazole derivatives as selective
                          phosphodiesterase 4 inhibitors
INVENTOR(S):              Hopper, Allen; Dunn, Robert F.; Kuester, Erik Mikal;
                          Conticello, Richard D.
PATENT ASSIGNEE(S):       Memory Pharmaceuticals Corporation, USA
SOURCE:                   PCT Int. Appl., 221 pp.
```

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006044528	A1	20060427	WO 2005-US36801	20051014
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005295753	A1	20060427	AU 2005-295753	20051014
CA 2584317	A1	20060427	CA 2005-2584317	20051014
US 20060154960	A1	20060713	US 2005-249769	20051014
US 7432266	B2	20081007		
EP 1799673	A1	20070627	EP 2005-816308	20051014
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008516964	T	20080522	JP 2007-536876	20051014
CN 101166733	A	20080423	CN 2005-80043196	20070615
US 20080207660	A1	20080828	US 2008-108833	20080424

PRIORITY APPLN. INFO.: US 2004-618725P P 20041015
US 2005-249769 A3 20051014
WO 2005-US36801 W 20051014

OTHER SOURCE(S): MARPAT 144:432795
GI



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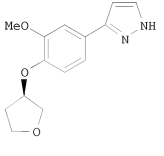

II

AB Title (hetero)aryl pyrazole compds. I [wherein Ar = substituted Ph, pyridinyl, benzo-furanyl, benzo-pyrazolyl, pyrazolo[4,3-b]pyridinyl; L = bond, (CH2)nCONH, (CH2)nNHCO, (CH2)nCONHSO2, (CH2)nSO2NH, (CH2)nSO2, (CH2)nCO2, (un)substituted alkylene optionally interrupted by O, NH, S; n = 0-3; R3 = H, (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl; R7, R8 = independently H, halo, (un)substituted alkyl, alkenyl, alkynyl; and pharmaceutically acceptable salts thereof] were prepared The invention compds. exhibited improved phosphodiesterase 4 (PDE4) inhibition as compared to compds. such as rolipram and showed selectivity with regard to inhibition of other

classes of PDEs. For example, 3-hydroxy-4-methoxy-benzaldehyde was condensed with (S)-3-hydroxy-tetrahydrofuran using PPh3 and DIAD in THF to give (R)-4-methoxy-3-[(tetrahydrofuran-3-yl)oxy]benzaldehyde (66%). Reaction of the aldehyde with diethoxyphosphorylacetaldehyde tosyl-hydrazone in the presence of NaH in THF provided the desired pyrazole II (57%). Compds. of the invention blocked the human PDE4 mediated conversion of cAMP to adenosine with IC50 values ranging from 10 nM to 5000 nM. Thus, I and their pharmaceutical compns. are useful for enhancing cognition and treating psychosis, allergic conditions, or inflammatory disease, Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Pick's disease, Cretuzfeldt-Jakob disease, HIV, cardiovascular disease, head trauma or age-related cognitive decline, schizophrenia, bipolar or manic depression, major depression, drug addiction or morphine dependence (no data).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 31 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1018151 CAPLUS

DOCUMENT NUMBER: 143:278260

TITLE: Phosphodiesterase inhibitors for cognitive enhancement

AUTHOR(S): Rose, Gregory M.; Hopper, Allen; De Vivo, Michael; Tehim, Ashok

CORPORATE SOURCE: Memory Pharmaceuticals Corp., Montvale, NJ, 07645, USA

SOURCE: Current Pharmaceutical Design (2005), 11(26), 3329-3334
CODEN: CPDEFP; ISSN: 1381-6128

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. An effective treatment for age-related cognitive deficits remains an unmet medical need. Currently available drugs for the symptomatic treatment of Alzheimer's disease or other dementias have limited efficacy. This may be due to their action at only one of the many neurotransmitter systems involved in the complex mechanisms that underlie cognition. An alternative approach would be to target second messenger systems that are utilized by multiple neurotransmitters. CAMP is a second messenger that plays a key role in biochem. processes that regulate the cognitive process of memory consolidation. Prolongation of cAMP signals can be accomplished by inhibiting phosphodiesterases (PDEs). Eleven PDE families, comprised of more than 50 distinct members, are currently known. This review summarizes the evidence demonstrating that rolipram, a selective inhibitor of cAMP-selective PDE4 enzymes, has pos. effects on learning and memory in animal models. These data provide support for the general approach of second messenger modulation as a potential therapy for cognitive dysfunction, and specifically suggest that PDE4 inhibitors may have utility for improving the symptoms of cognitive decline associated with neurodegenerative and psychiatric diseases.

OS.CITING REF COUNT: 40 THERE ARE 40 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)

REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 32 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:965063 CAPLUS

DOCUMENT NUMBER: 141:410960

TITLE: Preparation of 8-(3-biaryl)phenylquinoline phosphodiesterase-4 inhibitors

INVENTOR(S): Dube, Daniel; Dube, Laurence; Gallant, Michel; Lacombe, Patrick; Deschenes, Denis; MacDonald, Dwight
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004096220	A1	20041111	WO 2004-CA622		20040427
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004234190	A1	20041111	AU 2004-234190		20040427
CA 2523336	A1	20041111	CA 2004-2523336		20040427
EP 1635829	A1	20060322	EP 2004-729586		20040427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
CN 1812787	A	20060802	CN 2004-80018346		20040427
CN 100441185	C	20081210			
JP 2006524638	T	20061102	JP 2006-504121		20040427
US 20060223850	A1	20061005	US 2005-554176		20051021
US 7482456	B2	20090127			
IN 2005DN04934	A	20070928	IN 2005-DN4934		20051027
PRIORITY APPLN. INFO.:			US 2003-466542P	P	20030430
			WO 2004-CA622	W	20040427

OTHER SOURCE(S): MARPAT 141:410960
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title 8-phenylquinolines I [S1-S3 = H, OH, halo, alkyl, etc.; R1 = CO2aryl, CONHaryl, CONHheteroaryl, etc.; Ar1, Ar2 = (hetero)aryl or an N-oxide thereof; R2 = H, aryl, haloaryl, heterocyclyl, etc.; R3 = H, alkyl, hydroxyalkyl, etc.; R4 = H, halo, CN, alkyl, etc.] which are PDE4 inhibitors, were prepared E.g., a multi-step synthesis of II (no characterization data given for intermediates), which showed IC50 of 0.155 μM in LPS and FMLP-induced TNF-α and LTB4 assays in human whole blood, was given. The pharmaceutical compns. comprising the compound I are claimed.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 33 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:927199 CAPLUS
DOCUMENT NUMBER: 141:379922

TITLE: Preparation of pyrazole derivatives as selective phosphodiesterase 4 inhibitors

INVENTOR(S): Hopper, Allen; Kuester, Erik; Dunn, Robert; Conticello, Richard

PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 186 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094411	A1	20041104	WO 2004-US11899	20040416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004232973	A1	20041104	AU 2004-232973	20040416
CA 2522687	A1	20041104	CA 2004-2522687	20040416
US 20040229918	A1	20041118	US 2004-825611	20040416
US 7226930	B2	20070605		
EP 1631568	A1	20060308	EP 2004-759965	20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004009888	A	20060523	BR 2004-9888	20040416
CN 1809559	A	20060726	CN 2004-80017033	20040416
JP 2006523719	T	20061019	JP 2006-513094	20040416
MX 2005011200	A	20051214	MX 2005-11200	20051018
IN 2005DN04777	A	20070817	IN 2005-DN4777	20051019
US 20070203197	A1	20070830	US 2007-797151	20070501
US 7495017	B2	20090224		
US 20090221661	A1	20090903	US 2009-389873	20090220

PRIORITY APPLN. INFO.:

US 2003-463725P	P	20030418
US 2004-825611	A3	20040416
WO 2004-US11899	W	20040416
US 2007-797151	A1	20070501

OTHER SOURCE(S): MARPAT 141:379922

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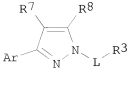

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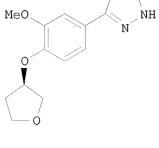

II

AB Title (hetero)aryl pyrazole compds. I [wherein Ar = substituted Ph, pyridinyl, benzofuranyl, benzopyrazolyl, pyrazolo[4,3-b]pyridinyl; L = bond, (CH2)nCONH, (CH2)nCON(alkyl), (CH2)nNHCO, (CH2)nCONHSO2, (CH2)nSO2NH, (CH2)nSO2, (CH2)nCO2, (un)substituted alkylene optionally interrupted by O, NH, S; n = 0-3; R3 = H, (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl; R7, R8 = independently H, halo, (un)substituted alkyl, alkenyl, alkynyl; and pharmaceutically acceptable salts thereof] were prepared The invention compds. exhibited improved phosphodiesterase 4 (PDE4) inhibition as compared to compds. such as rolipram and showed selectivity with regard to inhibition of other classes of PDEs. For example, 3-hydroxy-4-methoxybenzaldehyde was condensed with (S)-3-hydroxytetrahydrofuran using PPh3 and DIAD in THF to give (R)-4-methoxy-3-[(tetrahydrofuran-3-yl)oxy]benzaldehyde (66%). Reaction of the aldehyde with diethoxyphosphorylacetaldehyde tosylhydrazone in the presence of NaH in THF provided the desired pyrazole II (57%). Compds. of the invention blocked the human PDE4 mediated conversion of cAMP to adenosine with IC50 values ranging from 10 nM to 5000 nM. Thus, I and their pharmaceutical compns. are useful for enhancing cognition and treating psychosis, allergic conditions, or inflammatory disease (no data).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 34 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:927168 CAPLUS

DOCUMENT NUMBER: 141:395413

TITLE: Preparation of 4-(substituted-phenyl)-2-pyrrolidinone derivatives as selective phosphodiesterase 4 inhibitors

INVENTOR(S): Tehim, Ashok; Hopper, Allen; Liu, Ruiping; Kuester, Erik; Dunn, Robert F.; Renau, Thomas E.

PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA; Hoffmann La-Roche Inc.

SOURCE: PCT Int. Appl., 195 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094375	A2	20041104	WO 2004-US11765	20040416
WO 2004094375	A3	20050421		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004232958	A1	20041104	AU 2004-232958	20040416
CA 2522631	A1	20041104	CA 2004-2522631	20040416
US 20050026913	A1	20050203	US 2004-825610	20040416

EP 1613590	A2	20060111	EP 2004-750220		20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
BR 2004010235	A	20060509	BR 2004-10235		20040416
CN 1805929	A	20060719	CN 2004-80016778		20040416
JP 2006523710	T	20061019	JP 2006-510117		20040416
MX 2005011055	A	20061207	MX 2005-11055		20051014
KR 2006039392	A	20060508	KR 2005-719778		20051017
IN 2005DN04695	A	20070928	IN 2005-DN4695		20051017
PRIORITY APPLN. INFO.:			US 2003-463054P	P	20030416
			WO 2004-US11765	W	20040416

OTHER SOURCE(S): MARPAT 141:395413

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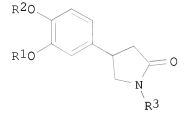

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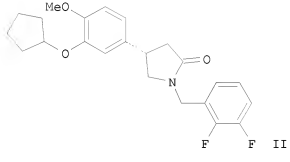


II

AB Title pyrrolidinones compds. I [R1 = alkyl, wherein optionally 1 or more CH2CH2 groups are replaced by CH:CH or C.tplbond.C, (un)substituted cycloalkyl, aryl, arylalkyl, arylalkenyl, (un)saturated heterocyclyl, heterocyclylalkyl, etc.; R2 = (un)substituted alkyl; R3 = C(:O)R4; CH2CO2R5, (CH2)nSR5, etc.; R4 = (un)substituted alkoxyalkyl, cycloalkyl, aryl, arylalkyl, etc.; R5 = H, (un)substituted alkoxy/alkyl, cycloalkyl, aryl, etc.] were prepared The invention compds. exhibited improved phosphodiesterase 4 (PDE4) inhibition as compared to compds. such as rolipram and showed selectivity with regard to inhibition of other classes of PDEs. For example, reacting 4-(3-cyclopentyloxy-4-methoxyphenyl)-2-pyrrolidinone with 2,3-difluorobenzyl bromide gave II in 70% yield. Selected I blocked the human PDE4 mediated conversion of cAMP to adenosine with IC50 values < 10 nM. Thus, I and their pharmaceutical compns. are useful for enhancing cognition and treating psychosis, allergic conditions, or inflammatory disease (no data).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:857402 CAPLUS
DOCUMENT NUMBER: 141:325764
TITLE: Growth hormone secretagogue-phosphodiesterase 4 inhibitor combination for the treatment of Alzheimer's disease
INVENTOR(S): Castro Pineiro, Jose Luis
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004087157	A2	20041014	WO 2004-GB1435	20040401
WO 2004087157	A3	20041118		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004226698	A1	20041014	AU 2004-226698	20040401
CA 2521046	A1	20041014	CA 2004-2521046	20040401
CN 1764457	A	20060426	CN 2004-80008035	20040401
EP 1660086	A2	20060531	EP 2004-725099	20040401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2006522084	T	20060928	JP 2006-506077	20040401
US 20060183764	A1	20060817	US 2005-552367	20051003
IN 2005DN04491	A	20071012	IN 2005-DN4491	20051004

PRIORITY APPLN. INFO.: GB 2003-7863 A 20030404
WO 2004-GB1435 A 20040401

AB The invention discloses the treatment or prevention of diseases involving deposition of β-amyloid in the brain, e.g. Alzheimer's disease, via the combined administration of a growth hormone secretagogue and a PDE4 inhibitor.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 36 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:756612 CAPLUS
DOCUMENT NUMBER: 141:277367
TITLE: Preparation of diphenylethylene compounds as PDE4 inhibitors for treatment of cancer, CNS disorders, and inflammatory disorders
INVENTOR(S): Muller, George W.; Payvandi, Faribourz; Zhang, Ling H.; Robarge, Michael J.; Chen, Roger; Man, Hon-Wah
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 218 pp.

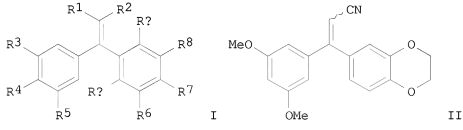
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078144	A2	20040916	WO 2004-US6781	20040305
WO 2004078144	A3	20041209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004218364	A1	20040916	AU 2004-218364	20040305
CA 2517886	A1	20040916	CA 2004-2517886	20040305
EP 1603864	A2	20051214	EP 2004-718007	20040305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008005	A	20060214	BR 2004-8005	20040305
CN 1780811	A	20060531	CN 2004-80011822	20040305
JP 2006519874	T	20060831	JP 2006-509173	20040305
ZA 2005007321	A	20070328	ZA 2005-7321	20040305
CN 101053558	A	20071017	CN 2007-10101369	20040305
NZ 542407	A	20080829	NZ 2004-542407	20040305

PRIORITY APPLN. INFO.:

US 2003-452460P	P	20030305
CN 2004-80011822	A3	20040305
WO 2004-US6781	A	20040305

OTHER SOURCE(S): MARPAT 141:277367
GI



AB The invention relates to the preparation of title compds. I [wherein R1, R2 = independently H, CN, alkoxy(carbonyl), alkanoyl, carbamoyl, (un)substituted alkyl, alkenyl, alkynyl, aryl, heterocyclyl; Rc, Rd, R6-R8 = independently H, halo, CN, NO2, OH, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, alkoxy, amino, carboxy, carbamoyl, ureido, etc.; R3-R5 = independently halo, CN, NO2, OH, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, alkoxy, amino, carboxy, carbamoyl, ureido, etc.; and pharmaceutically acceptable salts, solvates, or hydrates thereof] as phosphodiesterase IV (PDE4) inhibitors (no data). For example, reductive addition of 6-bromo-2,3-dihydrobenzo[1,4]dioxin with 3,5-dimethoxybenzaldehyde gave (2,3-dihydrobenzo[1,4]dioxin-6-yl)(3,5-dimethoxyphenyl)methanol (91%), which was oxidized using activated MnO2 powder to the methanone (93%). Reaction of the methanone with cyanomethylphosphonic acid di-Et ester in the presence of lithium

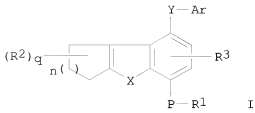
bis(trimethylsilyl)amide provided II (88%). The present invention also relates to methods for preventing or treating cancer, a CNS disorder, or an inflammatory disorder by administering one or more diphenylethylene compds. I optionally in combination with one or more other therapeutical agents. The present invention further relates to articles of manufacture and kits comprising I.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

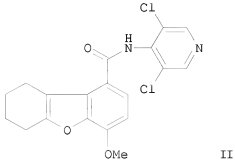
L7 ANSWER 37 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:675744 CAPLUS
DOCUMENT NUMBER: 141:207059
TITLE: Tricyclic compounds (dibenzofurans, dibenzothiophenes, carbazoles, and analogs) with PDE4 inhibitory activity, useful for the treatment of inflammatory and allergic disorders, process for their preparation, and methods of use
INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Bedekar, Sarika Suhas
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069831	A1	20040819	WO 2004-IB330	20040210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003MU00177	A	20050204	IN 2003-MU177	20030210
PRIORITY APPLN. INFO.:			IN 2003-MU177 A	20030210
OTHER SOURCE(S):	MARPAT 141:207059			

GI



I



II

AB The invention relates to novel heterocyclic compds. and their analogs, tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, pharmaceutically acceptable salts, appropriate oxides, and pharmaceutically acceptable solvates, as well as pharmaceutical compns. containing them. The invention more particularly relates to novel phosphodiesterase type 4 (PDE4) inhibitors. In particular, compds. I and their aforementioned related compds. are claimed [wherein: R1, R2, R3 = H, (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl(alkyl), heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, protecting groups, or two ortho R2 may form 3- to 7-membered ring with 0-2 optional NR1/O/S heteroatoms; X = O, S(O)m, NH, or NR5; Y = CONR4, NR4SO2, SO2NR4, and NR4CO; P = O or S; q = 0-5; n = 1-3; m = 0-2; Ar = (un)substituted aryl, arylalkyl, heterocyclic, or heteroaryl; R4 = H, (un)substituted alkyl, OH, OR1, aryl, or heterocyclic; R5 = (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, and protecting groups]. The compds. (33 examples) were prepared and tested for PDE4 inhibitory activity. For instance, 6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-carboxylic acid chloride [prepared in 5 steps from 2-methoxyphenol (guaicol) and 2-bromocyclohexanone] was amidated with 4-amino-3,5-dichloropyridine in DMF/THF to give invention compound II. This compound had an IC50 value of 0.4468 nM against PDE4 in vitro.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 38 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:467889 CAPLUS

DOCUMENT NUMBER: 141:38596

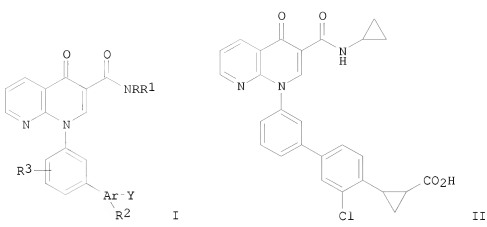
TITLE: Preparation of biphenylnaphthyridonecarboxamides as phosphodiesterase-4 inhibitors

INVENTOR(S): Dube, Daniel; Gallant, Michel; Lacombe, Patrick; Aspiotis, Renee; Dube, Laurence; Girard, Yves;

MacDonald, Dwight
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048374	A1	20040610	WO 2003-CA1800	20031119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506648	A1	20040610	CA 2003-2506648	20031119
AU 2003283167	A1	20040618	AU 2003-283167	20031119
AU 2003283167	B2	20090108		
EP 1565464	A1	20050824	EP 2003-775029	20031119
EP 1565464	B1	20080723		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016458	A	20051011	BR 2003-16458	20031119
CN 1738819	A	20060222	CN 2003-80108952	20031119
CN 100475813	C	20090408		
JP 2006508989	T	20060316	JP 2004-554102	20031119
RU 2312865	C2	20071220	RU 2005-119644	20031119
NZ 539812	A	20071221	NZ 2003-539812	20031119
AT 402175	T	20080815	AT 2003-775029	20031119
US 20050107402	A1	20050519	US 2004-764229	20040123
US 7238706	B2	20070703		
ZA 2005003586	A	20060726	ZA 2005-3586	20050505
US 20060058316	A1	20060316	US 2005-534582	20050511
US 7342024	B2	20080311		
MX 2005005413	A	20050803	MX 2005-5413	20050520
NO 2005003046	A	20050727	NO 2005-3046	20050621
PRIORITY APPLN. INFO.:			US 2002-428611P P	20021122
			WO 2003-CA1800 W	20031119

OTHER SOURCE(S): MARPAT 141:38596
GI



AB Title compds. [I; Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, imidazolyl; Y = CO2R4, ACO2R4, etc.; A = alkyl; R, R4 = H, alkyl; R1 = H, (substituted) alkyl, cycloalkyl, alkoxy, alkenyl, alkynyl, heteroaryl, heterocyclyl; R2 = H, halo, cyano, NO2, (substituted) alkyl, cycloalkyl, alkoxy, Ph, heteroaryl, amino, etc.; R3 = H, halo, cyano, NO2, (substituted) alkyl, cycloalkyl, etc.], were prepared Thus, title compound (II) (preparation outlined) inhibited PDE4-mediated hydrolysis of cAMP to AMP with IC50 = 0.1 nM.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 39 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:143155 CAPLUS

DOCUMENT NUMBER: 140:199339

TITLE: Preparation of 6-aminopurines and related compounds as selective phosphodiesterase-4 inhibitors for treatment of psychosis and inflammation

INVENTOR(S): Liu, Ruiping; Hopper, Allen T.; Tehim, Ashok; Hess, Hans-Jurgen E.; Rong, Yajing

PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

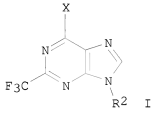
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014913	A2	20040219	WO 2003-US24914	20030808
WO 2004014913	A3	20040729		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,

	BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2494028	A1	20040219	CA 2003-2494028	20030808
AU 2003264017	A1	20040225	AU 2003-264017	20030808
EP 1529049	A2	20050511	EP 2003-785075	20030808
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1688580	A	20051026	CN 2003-823977	20030808
JP 2005538134	T	20051215	JP 2004-527913	20030808
US 20070093510	A1	20070426	US 2003-636979	20030808
US 7332486	B2	20080219		
US 20080139583	A1	20080612	US 2008-26198	20080205
PRIORITY APPLN. INFO.:			US 2002-401765P	P 20020808
			US 2003-636979	A1 20030808
			WO 2003-US24914	W 20030808

OTHER SOURCE(S): MARPAT 140:199339
GI



I

AB Title compds. I [X = NHR1; R1 = H, (un)substituted alkyl, cycloalkyl, etc.; R2 = (un)substituted aryl, heteroaryl, heteroarylalkyl, etc.,] and their pharmaceutically acceptable salts were prepared For example, electrophilic substitution of aminocyclopropane with compound I [X = Cl; R2 = 2-fluorobenzyl], e.g., prepared from 5-aminoimidazole-4-carboxamide hydrochloride in 3-steps, followed by acid work-up furnished compound I [R1 = cyclopropyl; R2 = 2-fluorobenzyl] methanesulfonate in 80.3% overall yield. In human PDE-4 inhibition assays, compds. I showed indicative (sic.) inhibition of PDE-4 activity (no data provided). Compds. I are claimed useful for the treatment of psychosis, Alzheimer's disease, allergy, inflammation, etc.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 40 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:80659 CAPLUS
DOCUMENT NUMBER: 140:146131
TITLE: Preparation of 6-amino-1H-indazole and 4-aminobenzofuran derivatives useful as phosphodiesterase 4 inhibitors
INVENTOR(S): Schumacher, Richard A.; Hopper, Allan T.; Tehim, Ashok
PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004009557	A1	20040129	WO 2003-US22401		20030718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 20030149052	A1	20030807	US 2003-361634		20030211
CA 2492911	A1	20040129	CA 2003-2492911		20030718
AU 2003256601	A1	20040209	AU 2003-256601		20030718
US 20040087584	A1	20040506	US 2003-622117		20030718
US 7153871	B2	20061226			
EP 1549619	A1	20050706	EP 2003-765684		20030718
EP 1549619	B1	20090121			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003013000	A	20050712	BR 2003-13000		20030718
CN 1668602	A	20050914	CN 2003-817233		20030718
CN 100381425	C	20080416			
JP 2006502995	T	20060126	JP 2004-523528		20030718
NZ 537725	A	20060831	NZ 2003-537725		20030718
NZ 547469	A	20071130	NZ 2003-547469		20030718
AT 421505	T	20090215	AT 2003-765684		20030718
CN 101423497	A	20090506	CN 2008-10108288		20030718
RU 2354648	C2	20090510	RU 2005-104820		20030718
ES 2323688	T3	20090723	ES 2003-765684		20030718
IN 2005DN00076	A	20081107	IN 2005-DN76		20050107
ZA 2005000436	A	20060726	ZA 2005-436		20050117
MX 2005000825	A	20050829	MX 2005-825		20050119
NO 2005000871	A	20050218	NO 2005-871		20050218
HK 1081194	A1	20080905	HK 2006-101282		20060127
US 20070078139	A1	20070405	US 2006-602283		20061121
US 20070123570	A1	20070531	US 2006-642592		20061221
PRIORITY APPLN. INFO.:			US 2002-396726P	P	20020719
			US 2001-262651P	P	20010122
			US 2001-267196P	P	20010208
			US 2001-306140P	P	20010719
			US 2002-51309	A3	20020122
			CN 2003-817233	A3	20030718
			NZ 2003-537725	A3	20030718
			US 2003-622117	A3	20030718
			WO 2003-US22401	W	20030718
			US 2004-754600	A3	20040112

OTHER SOURCE(S): MARPAT 140:146131
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention refers to new aminoindazole and aminobenzofuran derivs. of formula I and II [wherein: R1 = H, (un)substituted (cyclo/hetero)alkyl; R2 = H, (un)substituted alkyl; R3 = H, (un)substituted alkyl, arylalkyl, etc.; R4 = H, (un)substituted (hetero)aryl; R5 = (halo)alkoxy, (halo)alkylthio; R6 = (un)substituted -C(O)-alkyl, etc.] useful as phosphodiesterase 4 (PDE4) inhibitors. In vitro measurements of human type 4 phosphodiesterase inhibition activity and in vivo tests for

learning and memory (passive avoidance in rats and radial arm maze task in rats) were performed for compds. I and II. Compds. I and II are claimed to be useful for treatment of patients suffering from memory impairment due to Alzheimer's diseases, schizophrenia, Parkinson's disease, etc. For instance, indazole III (example 4) was prepared from 3-pyridinecarboxaldehyde and aminoindazole IV via reductive amination, amination of 3-IC6H4CO2t-Bu by resultant amine V, and hydrolysis.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 41 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:80654 CAPLUS

DOCUMENT NUMBER: 140:128150

TITLE: Preparation of selective phosphodiesterase 4 inhibitors, including ether-functionalized N-substituted aniline and diphenylamine analogs, for cognition enhancement and other uses

INVENTOR(S): Schumacher, Richard A.; Hopper, Allen T.; Tehim, Ashok; Hess, Hans-Jurgen Ernst; Unterbeck, Axel; Kuester, Erik; Brubaker, William Frederick, Jr.; Dunn, Robert F.

PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009552	A1	20040129	WO 2003-US22543	20030721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2492907	A1	20040129	CA 2003-2492907	20030721
AU 2003256616	A1	20040209	AU 2003-256616	20030721
AU 2003256616	B2	20090827		
US 20050119225	A1	20050602	US 2003-622833	20030721
US 7405230	B2	20080729		
BR 2003012999	A	20050607	BR 2003-12999	20030721
EP 1539697	A1	20050615	EP 2003-765748	20030721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1688545	A	20051026	CN 2003-822354	20030721
JP 2006504656	T	20060209	JP 2004-523585	20030721
NZ 537724	A	20061027	NZ 2003-537724	20030721
RU 2368604	C2	20090927	RU 2005-104819	20030721
IN 2005DN00091	A	20060609	IN 2005-DN91	20050110
ZA 2005000488	A	20060628	ZA 2005-488	20050118
MX 2005000827	A	20050829	MX 2005-827	20050119
NO 20050000870	A	20050331	NO 2005-870	20050218
IN 2007DN04839	A	20070824	IN 2007-DN4839	20070622

US 20090048255	A1	20090219	US 2008-174714		20080717
PRIORITY APPLN. INFO.:			US 2002-396725P	P	20020719
			US 2003-622833	A3	20030721
			WO 2003-US22543	W	20030721
			IN 2005-DN91	A3	20050110

OTHER SOURCE(S): MARPAT 140:128150

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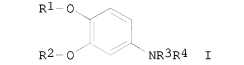

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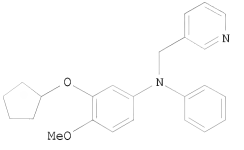

II

AB PDE4 inhibition (no data) is achieved by novel compds., e.g., ether-functionalized N-substituted aniline and diphenylamine analogs (shown as I; variables defined below; e.g. II). Although the methods of preparation are not claimed, >40 example prepns. are included. For example, II was prepared by arylation of N-[(3-pyridyl)methyl]-3-cyclopentyloxy-4-methoxyaniline by iodobenzene using NaOtBu, Pd2dba3, and PtBu3 in toluene. In a 'passive avoidance in rats' test, an in vivo test for learning and memory, the amnesic effect of MK-801 is reversed in a statistically significant manner by actual test compds. in a dose-dependent fashion [e.g., 3-cyclopentyloxy-4-methoxy-N-(3-pyridylmethyl)diphenylamine, ED range = 0.5 to 2.5 mg/kg, i.p.; and N-(3-cyclopentyloxy-4-methoxyphenyl)-N-(3-pyridylmethyl)-3-aminobenzoic acid, ED range = 0.1 to 2.5 mg/kg, i.p.]. In a 'radial arm maze task in rats' test, an in vivo test for learning and memory, the amnesic effect of MK-801 on working memory is reversed in a statistically significant manner by the administration of actual test compds. in a dose-dependent fashion [e.g., 3-cyclopentyloxy-4-methoxy-N-(3-pyridylmethyl)diphenylamine, ED = 2.5 mg/kg, i.p.; p<0.01]. For I: R1 is H, alkyl having 1-4 C atoms (un)substituted by ≥1 halo; R2 is C1-12 alkyl, C3-10 cycloalkyl, C4-16 cycloalkylalkyl, C6-14 aryl, C6-14-aryl-C1-5-alkyl, a partially unsatd. carbocyclic group having 5-14 C atoms, a C5-10 heterocyclic group, or a heterocycle-alkyl group; R3 is H, C1-8 alkyl, a partially unsatd. carbocycle-alkyl group, C7-19-aryl-C1-5-alkyl, or heteroarylalkyl; R4 is H, C3-10 cycloalkyl, C6-14 aryl, or heteroaryl having 5-10 ring atoms; addnl. details are given in the claims.

OS.CITING REF COUNT:	4	THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 42 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:2860 CAPLUS

DOCUMENT NUMBER: 140:59526
TITLE: Preparation of 8-(biaryl)quinolines as PDE4 inhibitors
INVENTOR(S): Deschenes, Denis; Dube, Daniel; Dube, Laurence; Gallant, Michel; Girard, Yves; Lacombe, Patrick; MacDonald, Dwight
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000814	A1	20031231	WO 2003-CA957	20030623
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2490043	A1	20031231	CA 2003-2490043	20030623
AU 2003243870	A1	20040106	AU 2003-243870	20030623
AU 2003243870	B2	20081120		
EP 1517895	A1	20050330	EP 2003-760540	20030623
EP 1517895	B1	20070314		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006502104	T	20060119	JP 2004-514482	20030623
AT 356808	T	20070415	AT 2003-760540	20030623
ES 2282667	T3	20071016	ES 2003-760540	20030623
US 20050234238	A1	20051020	US 2004-517416	20041208
US 7153968	B2	20061226		

PRIORITY APPLN. INFO.:
US 2002-391364P P 20020625
US 2002-428313P P 20021122
WO 2003-CA957 W 20030623

OTHER SOURCE(S): MARPAT 140:59526
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein A = C or N; X = Ph, pyridyl, pyrazinyl, thiaphenyl, quinolinyl, benzofuranyl, oxadiazolyl, diazolylpyridinyl, imidazolylpyridinyl, oxadiazolylphenyl, benzodioxolyl; R1 = H, halo, or (un)substituted alkanoyl, cyclo/alkyl, alkenyl; R2, R3 = independently H, halo, OH, CN, NO2, or dialkenyl/dicycloalkyl/alkyl, alkenyl, wide variety of C-containing and heteroat. groups and/or functional groups optionally linked by C1-4alkyl; R2 optionally forms a double bond with an adjoining bond; R4 = H, halo; any ring nitrogen optionally forms N-oxide and N-chloride; and pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors. For example, II was prepared by Suzuki cross-coupling of quinoline III with 2-bromo-3-chlorothiophene. One hundred fifty-five invention compds.

suppressed PDE4 with IC50 values ranging from 36 μM to 0.005 μM in assays evaluating LPS- and FMLP-induced inhibition of tumor necrosis factor α (TNF-α) and leukotriene B4 (LTB4) in human whole blood. In a test measuring IgE-mediated allergic pulmonary inflammation induced by inhalation of antigen by sensitized guinea pigs, administration of I resulted in a significant reduction in the eosinophilia and the accumulation of other inflammatory leukocytes and effected less inflammatory lung damage. One hundred fifty-five invention compds. also inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC50 values ranging from 160 nM to 0.086 nM. Thus, I and their pharmaceutical compns. are useful for the treatment or prevention of a variety of allergic, inflammatory, CNS, and other conditions (no data).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 43 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:757679 CAPLUS

DOCUMENT NUMBER: 139:276825

TITLE: Preparation of 8-arylquinoline PDE4 inhibitors

INVENTOR(S): Gallant, Michel; Lacombe, Patrick; Dube, Daniel; Deschenes, Denis; MacDonald, Dwight; Dube, Laurence

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 184 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078397	A1	20030925	WO 2003-CA374	20030317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479069	A1	20030925	CA 2003-2479069	20030317
AU 2003209896	A1	20030929	AU 2003-209896	20030317
EP 1487797	A1	20041222	EP 2003-744288	20030317
EP 1487797	B1	20090527		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 432261	T	20090615	AT 2003-744288	20030317
US 20050245513	A1	20051103	US 2004-508261	20040917
US 7144896	B2	20061205		

PRIORITY APPLN. INFO.:			US 2002-365088P	P 20020318
			WO 2003-CA374	W 20030317

OTHER SOURCE(S): MARPAT 139:276825

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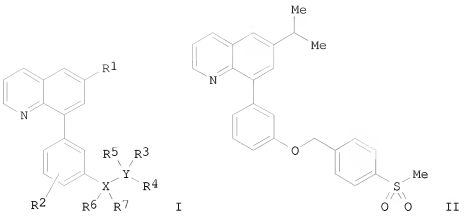


I II

AB Title compds. I [wherein R1 = H, halo, or (un)substituted alkanoyl, (cyclo)alkyl, alkenyl, alkoxy, (hetero)aryl, CN, heterocycloalkyl, carbamoyl, sulfamoyl, etc.; R2 = H, halo, OH, or (un)substituted alkyl or alkoxy; R3 = absent or H, CO2H, or (un)substituted (cycloalkyl)alkyl, alkanoyl, benzoyl, carbamoyl, etc.; R4 = (un)substituted Ph, pyrazolopyrimidinyl, benzothiazolyl, quinazolinyl, or heteroaryl; R5 = absent or H; R6 = absent, H, or alkyl; R7 = absent or H; X = O, S, N, C, or CO; wherein when X = O, S, or CO, then R6 and R7 are absent and when X = N, then R7 is absent; Y = C, S, N, SO2, O, or CO; wherein when Y = S, SO2, O, or CO, then R3 and R5 are absent and when Y = N, then R5 is absent; and pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors. For example, 3-(6-isopropylquinolin-8-yl)phenol was coupled with 1-chloromethyl-4-methanesulfonylbenzene in acetone to give II. One hundred sixteen invention compds. suppressed PDE4 with IC50 values ranging from 80 μM to 0.029 μM in assays evaluating LPS- and FMLP-induced inhibition of tumor necrosis factor α (TNF-α) and leukotriene B4 (LTB4) in human whole blood. In a test measuring IgE-mediated allergic pulmonary inflammation induced by inhalation of antigen by sensitized guinea pigs, administration of I resulted in a significant reduction in the eosinophilia and the accumulation of other inflammatory leukocytes and effected less inflammatory lung damage. One hundred forty-one invention compds. also inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC50 values ranging from 150 nM to 0.056 nM. Thus, I and their pharmaceutical compns. are useful for the treatment or prevention of a variety of allergic, inflammatory, CNS, and other conditions (no data).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 44 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:656587 CAPLUS

DOCUMENT NUMBER: 139:197374

TITLE: Preparation of nicotinamides useful as PDE4 inhibitors for treating diseases including inflammatory, allergic and respiratory diseases

INVENTOR(S): Bailey, Simon; Gautier, Elisabeth Colette Louise; Henderson, Alan John; Magee, Thomas Victor; Marfat, Anthony; Mathias, John Paul; McLeod, Dale Gordon; Monaghan, Sandra Marina; Stammen, Blanda Luzia Christa

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

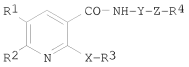
SOURCE: PCT Int. Appl., 266 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068235	A1	20030821	WO 2003-IB439	20030203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475712	A1	20030821	CA 2003-2475712	20030203
AU 2003245711	A1	20030904	AU 2003-245711	20030203
EP 1476158	A1	20041117	EP 2003-739392	20030203
EP 1476158	B1	20071114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007564	A	20041221	BR 2003-7564	20030203
JP 2005522450	T	20050728	JP 2003-567417	20030203
CN 1652782	A	20050810	CN 2003-808186	20030203
NZ 534197	A	20070126	NZ 2003-534197	20030203
AT 378049	T	20071115	AT 2003-739392	20030203
ES 2292988	T3	20080316	ES 2003-739392	20030203
US 20030220361	A1	20031127	US 2003-360100	20030206
US 20030220366	A1	20031127	US 2003-361062	20030206
US 6949573	B2	20050927		
US 20040224975	A1	20041111	US 2004-865263	20040609
US 7060717	B2	20060613		
IN 2004DN02070	A	20050401	IN 2004-DN2070	20040719
MX 2004007737	A	20041015	MX 2004-7737	20040810
NO 2004003793	A	20041021	NO 2004-3793	20040910
US 20060014780	A1	20060119	US 2005-229395	20050916
ZA 2004005803	A	20060531	ZA 2004-5803	20060316

PRIORITY APPLN. INFO.:		
GB 2002-3196	A	20020211
GB 2002-20999	A	20020910
GB 2002-24453	A	20021021
GB 2002-27139	A	20021120
US 2002-361991P	P	20020305
GB 2002-20984	A	20020910
US 2002-414247P	P	20020926
US 2002-414304P	P	20020926
GB 2002-24454	A	20021021
US 2002-425406P	P	20021112
US 2002-425474P	P	20021112
GB 2002-27140	A	20021120
US 2002-433330P	P	20021213
US 2002-433336P	P	20021213
WO 2003-IB439	W	20030203
US 2003-361062	A3	20030206
US 2004-865263	A1	20040609

OTHER SOURCE(S): MARPAT 139:197374
GI



I

AB The invention relates to nicotinamides (shown as I; variables defined below; e.g. anti-2-(benzo[1,3]dioxol-5-yloxy)-N-[4-(2-hydroxybenzoylamino)cyclohexyl]nicotinamide) and to processes for the preparation of, intermediates used in the preparation of, compns. containing and the uses of, such derivs. The nicotinamide derivs. according to the present invention are phosphodiesterase-4 inhibitors and are useful in numerous diseases, disorders and conditions, in particular inflammatory, allergic, respiratory diseases, disorders and conditions, as well as wounds. For I: R1 and R2 = H, halo, cyano, (C1-C4)alkyl and (C1-C4)alkoxy; X is -O-, -S- or -NH-; R3 = Ph, naphthyl, heteroaryl and (C3-C8)cycloalkyl or the bicyclic groups benzodioxol-5-yl, benzofuran-5-yl, benzofuran-6-yl, indan-5-yl; Y = 4-HNcyclohexyl, piperidin-1,4-diyl, 8-azabicyclo[3.2.1]octane-3,8-diyl, and 4-R5Ncyclohexyl wherein in each the N is bonded to Z in I and R5 = (C1-C4)alkyl and phenyl(C1-C4)alkyl. Z = C(O), C(O)NH, SO2, SO2NH, C(O)CH2NHSO2, SO2NHC(O), C(O)CH2NHC(O) wherein the left end is bonded to Y and the other end to R4; or alternatively Y-Z together = 4-NHC(O)cyclohexyl; R4 = Ph, naphthyl heteroaryl and (C3-C8)cycloalkyl, (un)substituted (C1-C6)alkyl; addnl. details including provisos are given in the claims. The antiinflammatory properties of 72 examples of I are demonstrated by their ability to inhibit TNFα release from human peripheral blood mononuclear cells, e.g. IC50 = 0.014 nM for syn-2-(3,4-difluorophenoxy)-5-fluoro-N-[4-(2-hydroxy-5-methylbenzoylamino)cyclohexyl]nicotinamide. About 200 example prepns. of I and 75 of intermediates are included. For example, to prepare anti-2-[(benzo[1,3]dioxol-5-yl)oxy]-N-[4-[(2-hydroxybenzoyl)amino]cyclohexyl]nicotinamide (160.7 mg), 2-hydroxybenzoic acid (0.767 mmol), 1-hydroxybenzotriazole hydrate (1.15 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.15 mmol) were stirred in DMF (5 mL) under an atmospheric of N2 at room temperature for 1.5 h. Anti-N-(4-aminocyclohexyl)-2-[(benzo[1,3]dioxol-5-yl)oxy]nicotinamide hydrochloride (0.767 mmol; preparation given) and N-methylmorpholine (0.767 mmol) were then added, and the reaction mixture stirred at room temperature for a further 18 h.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 45 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:656584 CAPLUS

DOCUMENT NUMBER: 139:197372

TITLE: Preparation of nicotinamides as phosphodiesterase-4 inhibitors for the treatment of diseases including inflammatory, allergic and respiratory diseases

INVENTOR(S): Magee, Thomas Victor

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068232	A1	20030821	WO 2003-IB377	20030203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475708	A1	20030821	CA 2003-2475708	20030203
AU 2003202116	A1	20030904	AU 2003-202116	20030203
EP 1476157	A1	20041117	EP 2003-700974	20030203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007574	A	20041221	BR 2003-7574	20030203
JP 2005522449	T	20050728	JP 2003-567414	20030203
US 20030191158	A1	20031009	US 2003-360122	20030206
US 20030195233	A1	20031016	US 2003-361083	20030206
US 6756392	B2	20040629		
MX 2004007736	A	20041015	MX 2004-7736	20040810
PRIORITY APPLN. INFO.:			GB 2002-3193 A	20020211
			US 2002-362154P P	20020305
			WO 2003-IB377 W	20030203

OTHER SOURCE(S): MARPAT 139:197372

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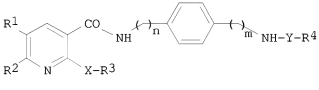

I

AB The invention relates to nicotinamides (shown as I; variables defined below; e.g. 2-(4-fluorophenoxy)-N-[4-[(2-hydroxy-3-methylbenzoylamino)methyl]benzyl]nicotinamide) and to processes for the preparation of, compns. containing and the uses of, such derivs. The nicotinamides are phosphodiesterase-4 inhibitors and are useful in numerous diseases, disorders and conditions, in particular inflammatory, allergic and respiratory diseases, disorders and conditions as well as for wounds healing. Eighteen example prepns. of I and 10 of intermediates are included. For example, to prepare 2-(4-fluorophenoxy)-N-[4-[(2-hydroxy-3-methylbenzoylamino)methyl]benzyl]nicotinamide (80 mg), a solution of 2-hydroxy-3-methylbenzoic acid (0.773 mmol), 1-hydroxybenzotriazole (1.16 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.01 mmol), N-(4-aminomethylbenzyl)-5-fluoro-2-(4-fluorophenoxy)nicotinamide hydrochloride (0.773 mmol) (preparation described) and N-methylmorpholine (1.55 mmol) in DMF (6 mL) were stirred under N2 at room temperature for 18 h. All the examples were tested in an assay of inhibition of TNFα release from human peripheral blood mononuclear cells and found to have an IC50 <500 nM; most of the tested compds. have an IC50 <200 nM. For I: m = 0-3; n = 0-3; R1 and R2 = H, halo, cyano, (C1-C4)alkyl and (C1-C4)alkoxy; X is -O-,

-S- or -NH-; R3 = (a) Ph, naphthyl, heteroaryl and (C3-C8)cycloalkyl, each (un)substituted with 1 to 3 substituents each halo, cyano, (C1-C4)alkyl, (C1-C4)alkoxy, (C1-C4)thioalkyl, -C(O)NH2, - C(O)NH[(C1-C4)alkyl], hydroxy, -O-C(O)(C1-C4)alkyl, -C(O)-O-(C1-C4)alkyl and hydroxy (C1-C4)alkyl, or (b) the bicyclic groups benzodioxol-5-yl, benzofuran-5-yl, benzofuran-6-yl, indan-5-yl; Y = -C(O)-, -C(O)NH-, -SO2-, -SO2NH-, -C(O)CH2NHSO2-, -SO2NHC(O)-, -C(O)CH2NHC(O)- wherein the left-hand connection is to NH and the right-hand connection is to R4. R4 = (a) Ph, naphthyl and heteroaryl, each (un)substituted with 1 to 3 substituents = carboxylic acid, C(O)-O-(C1-C4)alkyl, halo, cyano, -C(O)NH2, (C1-C4)alkyl, (C1-C4)alkoxy, (C1-C4) haloalkyl, hydroxy, and hydroxy(C1-C4)alkyl, or (b) (C1-C4)alkyl (un)substituted with a hydroxy, carboxylic acid, C(O)-O-(C1-C4)alkyl, Ph, naphthyl or heteroaryl group wherein said Ph, naphthyl and heteroaryl are each (un)substituted with 1 to 3 substituents = carboxylic acid, C(O)O(C1-C4)alkyl, halo, cyano, -C(O)NH2, (C1-C4)alkyl or (C1-C4)alkoxy, (C1-C4)haloalkyl, hydroxy, and hydroxy(C1-C4)alkyl.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 46 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:319707 CAPLUS

DOCUMENT NUMBER: 138:321128

TITLE: Preparation of 4-(4-alkoxy-3-hydroxyphenyl)-2-pyrrolidinone derivatives as PDE-4 inhibitors for the treatment of neurological syndromes

INVENTOR(S): Liu, Ruiping; De Vivo, Michael; Hess, Hans-Jurgen Ernst; Hopper, Allen; Keuster, Erik; Tehim, Ashok

PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003032981	A1	20030424	WO 2002-US32834	20021016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2463469	A1	20030424	CA 2002-2463469	20021016
AU 2002335015	A1	20030428	AU 2002-335015	20021016
AU 2002335015	B2	20061102		
US 20030139406	A1	20030724	US 2002-270724	20021016
US 7235579	B2	20070626		
EP 1435944	A1	20040714	EP 2002-801710	20021016
EP 1435944	B1	20090930		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013660	A	20040824	BR 2002-13660	20021016

CN 1604776	A	20050406	CN 2002-825102		20021016
JP 2005508961	T	20050407	JP 2003-535784		20021016
NZ 532288	A	20051223	NZ 2002-532288		20021016
RU 2340600	C2	20081210	RU 2004-115333		20021016
KR 2009080573	A	20090724	KR 2009-714588		20021016
IN 2004DN00971	A	20050401	IN 2004-DN971		20040413
MX 2004003516	A	20040723	MX 2004-3516		20040415
ZA 2004002856	A	20050125	ZA 2004-2856		20040415
NO 2004002024	A	20040514	NO 2004-2024		20040514
US 20050272803	A1	20051208	US 2005-186958		20050722
IN 2008DN04357	A	20080815	IN 2008-DN4357		20080522
US 20090176799	A1	20090709	US 2008-325433		20081201
PRIORITY APPLN. INFO.:			US 2001-329314P	P	20011016
			US 2002-270724	A1	20021016
			WO 2002-US32834	W	20021016
			IN 2004-DN971	A3	20040413
			KR 2004-705475	A3	20040414
			US 2005-186958	A1	20050722

OTHER SOURCE(S): MARPAT 138:321128

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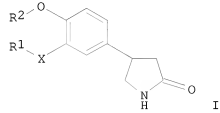

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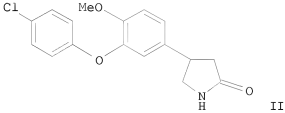

II

AB Title compds. I [X = O; R1 = alkyl, cycloalkyl, heterocyclic, etc.; R2 = alkyl; R3 = H, alkyl, cycloalkyl, arylalkyl, etc.] are prepared For instance, Me 3-(3-benzyloxy-4-methoxyphenyl)-4-nitrobutanoate is converted to 3-benzyloxy-4-methoxyphenyl (MeOH, NiCl6, NaBH4, 30 min, 0°) and subsequently debenzylated (MeOH/CH2Cl2, H2-10% Pd/C, 20 psi, 8 h). This intermediate is then coupled to 4-chlorophenylboronic acid (CH2Cl2, Cu(OAc)2, Et3N, 18 h) to give II. I exhibit improved PDE4 inhibition as compared to rolipram and show selectivity with regard to inhibition of other classes of PDEs.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 47 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:22685 CAPLUS

DOCUMENT NUMBER: 138:73184
TITLE: Preparation of substituted 8-arylquinoline phosphodiesterase-4 (PDE4) inhibitors
INVENTOR(S): Dube, Daniel; Girard, Yves; MacDonald, Dwight; Mastracchio, Anthony; Gallant, Michel; Lacombe, Patrick; Deschenes, Denis
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003002118	A1	20030109	WO 2002-CA953	20020626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2450686	A1	20030109	CA 2002-2450686	20020626
AU 2002344885	A1	20030303	AU 2002-344885	20020626
AU 2002344885	B2	20060629		
EP 1404330	A1	20040407	EP 2002-742600	20020626
EP 1404330	B1	20050601		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005501822	T	20050120	JP 2003-508357	20020626
AT 296630	T	20050615	AT 2002-742600	20020626
ES 2242036	T3	20051101	ES 2002-742600	20020626
US 20040162314	A1	20040819	US 2003-478791	20031125
US 6919353	B2	20050719		

PRIORITY APPLN. INFO.:		
US 2001-301220P	P	20010627
US 2001-303472P	P	20010706
WO 2002-CA953	W	20020626

OTHER SOURCE(S): MARPAT 138:73184
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 8-Arylquinolines (shown as I; variables defined below; e.g. both enantiomers of 4-hydroxy-1-{3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl}-2-(4-methanesulfonylphenyl)-4-methylpentan-3-one) wherein the aryl group at the 8-position contains a meta two atom bridge to an optionally substituted Ph or pyridyl group, are PDE4 inhibitors useful to treat asthma, chronic bronchitis, chronic obstructive pulmonary disease, arthritis, respiratory distress syndrome, allergic rhinitis, neurogenic inflammation, pain, rheumatoid arthritis, and other diseases. R1-R7 and Ar are as in claim 1. For I: Ar is Ph, pyridinone, pyridyl, or pyridyl N-oxide, optionally substituted with 1-5 independent -C1-6-alkyl, -OH, -CN, halogen, -CF3, -(C0-6-alkyl)-SOn-(C1-6-alkyl), -(C0-6-alkyl)-SOn-NH-(C1-6-alkyl) or 5-membered heteroaryl ring containing 1-4 heteroatoms = O, S or N, wherein the 5-membered-ring is optionally

substituted. R1 is H, halogen; or a -C1-6-alkyl, -cycloC3-6alkyl, -C1-6-alkenyl, -C0-4alkyl-C(O)-C0-4alkyl, -C1-6-alkoxy, aryl, heteroaryl, -CN, -heterocycloC3-6-alkyl, -amino, -C1-6-alkylamino, -(C1-6-alkyl)(C1-6-alkyl)amino, -C1-6-alkyl(oxy)C1-6-alkyl, -C(O)NH(aryl), -C(O)NH(heteroaryl), -SOnNH(aryl), -SOnNH(heteroaryl), -SOnNH(C1-6-alkyl), -C(O)N(C0-6alkyl)(C0-6-alkyl), -NH-SOn-(C1-6-alkyl), -carbamoyl, -(C1-6-alkyl)-O-C(CN)dialkylamino, or -(C0-6-alkyl)-SOn-(C1-6-alkyl) group, wherein any of the groups is optionally substituted with = 1-5 substituents. R2, R3, R6, and R7 = H, halogen, hydroxy, -C1-6-alkyl, or -C1-6-alkoxy, wherein the alkyl and alkoxy are optionally substituted independently with 1-3 halogen or OH; R4 is H, halogen, -CN, Ph, oxadiazolyl, or -C(O)-O-C0-6alkyl, wherein the alkyl and latter three possibilities are optionally substituted. R5 is H, hydroxy, -CN; or a -C1-6-alkyl, -C(O)C1-6alkyl, -C(O)aryl, -C(O)pyridyl, -C(O)-O-C0-6-alkyl, -C(O)-C3-7-cycloalkyl, -C1-6-alkyl-C3-7cycloalkyl, -C1-6-alkyl(C3-7-cycloalkyl)2, -C1-6-alkylaryl, -C(O)-N(C0-6alkyl)2, -SOnaryl, -SOn-C1-6-alkyl, -SOn-C3-7-cycloalkyl, -SOn-N(C0-6-alkyl)2, -P(O)(C1-6-alkyl)2, -P(O)(C1-6-alkoxy)2, Ph, pyridyl, -SOnimidazolyl, -SOnthiazolyl, 5-membered heteroaryl ring containing 1-4 heteroatoms = O, S or N or oxoisoxaphosphinanyl group, any of which group optionally substituted; or R5 and R6 form :O; or R6 and R3 form -CH2- or -O-; and n is 0-2. Although the methods of preparation are not claimed, >100 example prepns. are included. The IC50 values for PDE4 inhibition of Examples 1-113 generally are 0.02-26 μM as measured using LPS and FMLP-induced TNF-α and LTB4 assays in human whole blood. I were tested for effects on an IgE-mediated allergic pulmonary inflammation induced by inhalation of antigen by sensitized guinea pigs;. Administration of I (0.001-10 mg/kg i.p. or p.o.), up to three times during the 48 h following antigen challenge, lead to a significant reduction in the eosinophilia and the accumulation of other inflammatory leukocytes. There was also less inflammatory damage in the lungs of animals treated with I. Compds. which inhibit the hydrolysis of cAMP to AMP by the type-IV cAMP-specific phosphodiesterases were screened in a 96-well plate format; IC50 values of I generally ranged 0.1-25 nM.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 48 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:906219 CAPLUS

DOCUMENT NUMBER: 138:4594

TITLE: Preparation of 1-biaryl-[1,8]naphthyridin-4-one phosphodiesterase IV inhibitors for treatment of asthma and inflammation

INVENTOR(S): Guay, Daniel; Girard, Mario; Hamel, Pierre; Laliberte, Sebastien; Friesen, Richard; Girard, Yves; Li, Chun

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094823	A1	20021128	WO 2002-CA746	20020522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,				

PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2447765	A1	20021128	CA 2002-2447765	20020522
AU 2002257459	A1	20021203	AU 2002-257459	20020522
AU 2002257459	B2	20061214		
EP 1397359	A1	20040317	EP 2002-727127	20020522
EP 1397359	B1	20050831		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004534773	T	20041118	JP 2002-591496	20020522
AT 303384	T	20050915	AT 2002-727127	20020522
ES 2247325	T3	20060301	ES 2002-727127	20020522
US 20030096829	A1	20030522	US 2002-154591	20020524
US 6677351	B2	20040113		

PRIORITY APPLN. INFO.: US 2001-293247P P 20010524
WO 2002-CA746 W 20020522

OTHER SOURCE(S): MARPAT 138:4594

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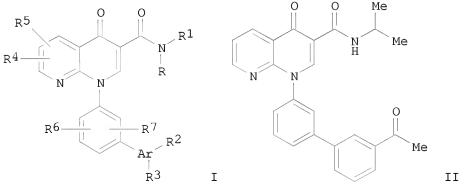


I II

AB Title compds. I [wherein Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, imidazolyl, or heteroaryl oxides; R = H or alkyl; R1 = H or (un)substituted (cyclo)alkyl, alkoxy, alkenyl, alkynyl, heteroaryl, or heterocyclyl; R2 = H, halo, (cyclo)alkyl, alkoxy, amino, acyl, alkoxycarbonyl, alkylsulfamoyl, alkylsulfonyl, or (un)substituted Ph, heteroaryl, or heterocyclyl, etc.; R3 = H, OH, NH2, halo, (un)substituted alkyl; R4-R7 = independently H, halo, NH2, or (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors for the treatment of asthma and inflammation. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate was cyclized using NaH in THF and the resulting ester saponified to give 1-(3-bromophenyl)-1,4-dihydro-[1,8]naphthyridin-4-one-3-carboxylic acid. Amidation with isopropylamine, followed by treatment with 3-acetylphenylboronic acid in the presence of trans-PdBr2(PPh3)2 and Na2CO3 in toluene and EtOH gave II. I demonstrated PDE4 inhibitory activity by suppression of TNF-α secretion in LPS stimulated human blood with IC50 values generally ranging from 0.005 μM to 15.4 μM. In a SPA based PDE activity assay, I inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC50 values between 34.3 nM and 134.0 nM.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 49 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:736215 CAPLUS
DOCUMENT NUMBER: 137:247488
TITLE: Preparation of C-organooxy- and N-substituted aniline and diphenylamine analogs as phosphodiesterase 4 inhibitors useful for enhancing cognition
INVENTOR(S): Hopper, Allen; Schumacher, Richard A.; Tehim, Ashok; De Vivo, Michael; Brubaker, William Frederick, Jr.; Liu, Ruiping; Hess, Hans-Juergen Ernst; Unterbeck, Axel
PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074726	A2	20020926	WO 2002-US1508	20020122
WO 2002074726	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2435847	A1	20020926	CA 2002-2435847	20020122
AU 2002303078	A1	20021003	AU 2002-303078	20020122
AU 2002303078	B2	20070830		
US 20020151566	A1	20021017	US 2002-51309	20020122
US 6699890	B2	20040302		
EP 1353907	A2	20031022	EP 2002-731078	20020122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003002793	A2	20031128	HU 2003-2793	20020122
HU 2003002793	A3	20060130		
EE 200300347	A	20031215	EE 2003-347	20020122
CN 1498211	A	20040519	CN 2002-807010	20020122
CN 100378075	C	20080402		
JP 2005507365	T	20050317	JP 2002-573735	20020122
JP 4223287	B2	20090212		
BR 2002006943	A	20060124	BR 2002-6943	20020122
NZ 527081	A	20060331	NZ 2002-527081	20020122
RU 2321583	C2	20080410	RU 2003-124303	20020122
US 20030149052	A1	20030807	US 2003-361634	20030211
US 20040087584	A1	20040506	US 2003-622117	20030718
US 7153871	B2	20061226		
BG 108003	A	20040930	BG 2003-108003	20030718
IN 2003DN01131	A	20070316	IN 2003-DN1131	20030718
NO 2003003288	A	20030922	NO 2003-3288	20030721
ZA 2003005623	A	20041117	ZA 2003-5623	20030721
KR 856622	B1	20080903	KR 2003-709624	20030721
MX 2003006519	A	20041015	MX 2003-6519	20030722
US 20040230072	A1	20041118	US 2004-754600	20040112

US 7205320	B2	20070417			
HK 1066215	A1	20080829	HK 2004-109061		20041117
US 20070078139	A1	20070405	US 2006-602283		20061121
IN 2008DN08577	A	20090515	IN 2008-DN8577		20081013
PRIORITY APPLN. INFO.:			US 2001-262651P	P	20010122
			US 2001-267196P	P	20010208
			US 2001-306140P	P	20010719
			US 2000-257196P	P	20001222
			US 2002-51309	A3	20020122
			US 2002-51390	A3	20020122
			WO 2002-US1508	W	20020122
			US 2002-396726P	P	20020719
			IN 2003-DN1131	A3	20030718
			US 2004-754600	A3	20040112

OTHER SOURCE(S): MARPAT 137:247488

AB Phosphodiesterase 4 (PDE4) inhibition is achieved by novel compds., 4-R1O-3-R2OC6H3NR3R4 (1, e.g., N-substituted aniline and diphenylamine analogs; e.g. 3-cyclopentyloxy-4'-ethyl-4-methoxy-N-(3-pyridylmethyl)diphenylamine). In 1, R1 is C1-4 alkyl unsubstituted or substituted one or more times by halogen. R2 is C1-12 alkyl, wherein optionally one or more -CH2CH2- groups is replaced in each case by -CH:CH- or -C.tplbond.C-, C3-10 cycloalkyl, C4-16 cycloalkylalkyl, C6-14 aryl , arylalkyl with C6-14 aryl and C1-5 alkyl, a partially unsatd. C5-14 carbocyclic group, a C5-10 heterocyclic group, which is saturated, partially saturated or unsatd., in which at least 1 ring atom is a N, O or S atom, or a heterocycloalkyl group with a C5-10 heterocyclic portion that is saturated, partially saturated or unsatd., in which at least 1 ring atom is a N, O or S atom, and a C1-5 alkyl portion. R3 is H, C1-8 (preferably C1-4) alkyl, a partially unsatd. carbocycle-alkyl group with a C5-14 carbocyclic portion and a C1-5 alkyl portion, C7-19 arylalkyl with C6-14 aryl and C1-5 alkyl, or heteroarylalkyl with C5-10 heteroaryl having at least 1 ring atom N, O or S atom and with C1-5 alkyl. R4 is H, C6-14 aryl or heteroaryl having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom. Addnl. restrictions on the values of R1-R4 are given in the claims. The amnesic effect of MK-801 on working memory in rats (radial arm maze task) is reversed in a statistically significant manner by the administration of actual test compds. in a dose-dependent fashion [e.g., 3-cyclopentyloxy-4-methoxy-N-(3-pyridylmethyl)diphenylamine, ED = 2.5 mg/kg, i.p.; p<0.01]. The amnesic effect of MK-801 on rats in a passive avoidance experiment is reversed in a statistically significant manner by actual test compds. in a dose-dependent fashion [e.g., 3-cyclopentyloxy-4-methoxy-N-(3-pyridylmethyl)diphenylamine, ED range = 0.5 to 2.5 mg/kg, i.p.; and N-(3-cyclopentyloxy-4-methoxyphenyl)-N-(3-pyridylmethyl)-3-aminobenzoic acid, ED range = 0.1 to 2.5 mg/kg, i.p.]. Although the methods of preparation are not claimed, .apprx.20 example prepns. are included and hundreds of compds. are listed in the claims.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 50 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:695783 CAPLUS

DOCUMENT NUMBER: 137:216886

TITLE: Preparation of 8-(alkenylaryl)quinoline phosphodiesterase-4 inhibitors

INVENTOR(S): Vailaya, Anant; Conlon, David A.; Ho, Guo-Jie; Macdonald, Dwight; Perrier, Helene; Thibert, Roch; Kwong, Elizabeth; Clas, Sophie-Dorothee

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Merck Frosst Canada & Co.

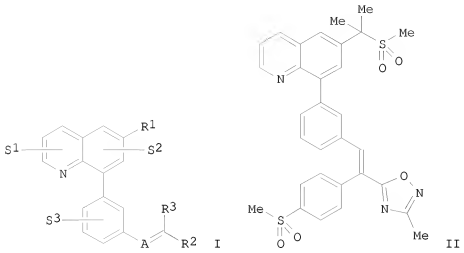
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069970	A1	20020912	WO 2001-US48674	20011214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20020143032	A1	20021003	US 2001-40993	20011109
US 6740666	B2	20040525		
CA 2431549	A1	20020912	CA 2001-2431549	20011214
AU 2001297603	A1	20020919	AU 2001-297603	20011214
AU 2001297603	B2	20060216		
EE 200300266	A	20031015	EE 2003-266	20011214
EP 1363635	A1	20031126	EP 2001-273908	20011214
EP 1363635	B1	20090415		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001016372	A	20031209	BR 2001-16372	20011214
HU 2004000654	A2	20040628	HU 2004-654	20011214
JP 2004521921	T	20040722	JP 2002-569145	20011214
CN 1551769	A	20041201	CN 2001-822760	20011214
NZ 526376	A	20050225	NZ 2001-526376	20011214
AT 428420	T	20090515	AT 2001-273908	20011214
BG 107900	A	20040630	BG 2003-107900	20030611
ZA 2003004672	A	20040421	ZA 2003-4672	20030617
NO 2003002807	A	20030815	NO 2003-2807	20030619
MX 2003005673	A	20031006	MX 2003-5673	20030619
IN 2003CN01089	A	20050422	IN 2003-CN1089	20030717

PRIORITY APPLN. INFO.: US 2000-256803P P 20001220
WO 2001-US48674 W 20011214

OTHER SOURCE(S): MARPAT 137:216886
GI



AB Title compds. I [wherein S1-S3 = independently H, OH, halo, NO2, CN, or (un)substituted alkyl or alkoxy; R1 = H, OH, halo, or (un)substituted acyl, (cyclo)alkyl, alkenyl, alkoxy, (hetero)aryl, heterocycloalkyl, NH2, carbamoyl, sulfamoyl , etc.; A = CH, C-ester, or CR4; R2 and R3 = independently H, halo, CN, CO2H, or (un)substituted (hetero)aryl, (heterocyclo)alkyl, alkoxy, acyl, carbamoyl, etc.; with the proviso that 1 of R2 and R3 must = (hetero)aryl; when R2 and R2 both = (hetero)aryl, then R2 and R3 may be optionally connected by a thio, oxy, or alkyl bridge to from a fused 3-ring system; R4 = CN or (un)substituted (hetero)aryl, alkyl, acyl, carbamoyl, etc.; or R2 or R3 may be optionally joined to R4 by a bond to form a ring; n = 0-2; and pharmaceutically acceptable H2SO4, methanesulfonic acid, p-toluenesulfonic acid, 2-naphthalenesulfonic acid, hydrochloride acid, or benzenesulfonic acid salts thereof] were prepared as phosphodiesterase-4 (PDE4) inhibitors. For example, a solution of (E)-1-(3-bromophenyl)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethene, diboron pinacol ester, [1,1'-bis(diphenylphosphino)ferrocene]PdCl2, and KOAc in DMF was stirred at 80° for 3 h. Sequential addition of 6-[1-methyl-1-(methylsulfonyl)ethyl]-8-bromoquinoline, [1,1'-bis(diphenylphosphino)ferrocene]PdCl2, and Na2CO3 followed by heating at 80° overnight gave (E)- and (Z)-II. Forty-two compds. of the invention exhibited IC50 values ranging from 0.04 μM to 8.71 μM in LPS and fMLP-induced TNF-α and LTB4 assays performed on human whole blood. All but one of same compds. inhibited the hydrolysis of cAMP to AMP by type-IV cAMP-specific phosphodiesterases with IC50 values ranging from 0.14 nM to 10.24 nM. Thus, I are useful as anti-inflammatory and anti-allergic agents for treatment of a wide variety of PDE4-related diseases and conditions (no data).

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 51 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:751595 CAPLUS

DOCUMENT NUMBER: 128:97573

ORIGINAL REFERENCE NO.: 128:18944h,18945a

TITLE: Rolipram and its optical isomers, phosphodiesterase 4 inhibitors, attenuated the scopolamine-induced impairments of learning and memory in rats

AUTHOR(S): Egawa, Takashi; Mishima, Kenichi; Matsumoto, Yoshiaki;

Iwasaki, Kiyo; Iwasaki, Katsunori; Fujiwara, Michihiro
CORPORATE SOURCE: Department of Physiology and Pharmacology, Faculty of Pharmaceutical Sciences, Fukuoka University, Fukuoka, 814-80, Japan
SOURCE: Japanese Journal of Pharmacology (1997), 75(3), 275-281
CODEN: JJPAAZ; ISSN: 0021-5198
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated the effects of (±)-rolipram, a phosphodiesterase (PDE) 4 inhibitor, and its isomers on scopolamine-induced deficits of learning and memory in rats using an 8-arm radial maze task and a passive avoidance task. 1) In the 8-arm radial maze task, (±)-rolipram (0.02-0.2 mg/kg, p.o.), (-)-rolipram (0.01.apprx.0.02 and 0.02.apprx.0.5 mg/kg, p.o.) and (+)-rolipram (20-50 mg/kg, p.o.) attenuated the scopolamine-induced deficits of spatial cognition. As for the min. ED of each drug, (-)-rolipram was 2 and 2000 times as (±)-rolipram and (+)-rolipram, resp. (-)-Rolipram produced a biphasic dose-response and (±)-rolipram produced a broad dose-response. 2) (±)-Rolipram and its isomers also attenuated the scopolamine-induced deficits in the passive avoidance response. Also for the min. ED, (.apprx.)-rolipram (0.01 .apprx. 0.02 mg/kg) was 2 and 200 times as potent as (±)-rolipram (0.02.apprx.0.1 mg/kg) and (+)-rolipram (2 mg/kg). 3) The behaviorally EDs of (±)-rolipram and its isomers also enhanced the oxotremorine-induced tremors in mice. Comparing these racemic isomers, (-)- and (±)-rolipram have more potent effects than (+)-rolipram on scopolamine-induced deficits in the 8-arm radial maze task and passive avoidance task. Especially (±)-rolipram has a wide dose range in these behavioral study. These results suggest that the ameliorating effects of rolipram might result from the indirect potentiation of various transmitters including cholinergic and noradrenergic systems by an increase in cAMP with the inhibition of PDE4.
OS.CITING REF COUNT: 36 THERE ARE 36 CAPLUS RECORDS THAT CITE THIS RECORD (36 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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